FIG. 1

peptide selection

peptide optimization

formation of Fc-peptide DNA construct

insertion of construct into expression vector

transfection of host cell with vector

expression of vector in host cell

Fc multimer formation in host cell

isolation of Fc multimer from host cell-

APPLN. NO: A-527H

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527H

FIG. 3A

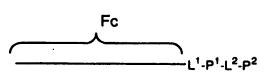


FIG. 3B

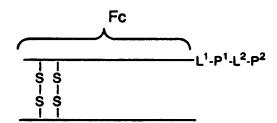


FIG. 3C

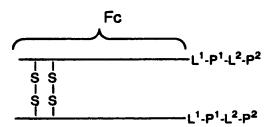


FIG. 4

	1	ATC	GAC	KAA:	VACT	CAC	CAC	ATG	rccz	ACCT	rtg:	CCZ	\GC1	rccc	GAA	CTC	CTG	GGG	GGA	CCG	TCA	
	-	TAC	CTC	TTI	TG	AGTO	STGT	rac.	\GG1	rgg <i>i</i>	AAC!	\GG1	CG	AGGC	CTI	GAG	GAC	ccc	CCT	GGC	AGT	60
a		M	D	ĸ	T	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	3	
	61	GTC	TTC	CTC	TTC	ccc	CC2	LAA	ACC	CAAC	GAG	CACC	CTC	CATO	ATC	TCC	CGG	ACC	CCT	'GAG		
	9.1	CAC	AAC	GAC	AAC	GGG	GGT	rrr	rggo	STTC	CTC	TGC	GA	TAC	TAC	AGC	GCC	TGG	GGA	CTC		120
a		v	F	L	F	P	P	K	P	ĸ	D	T	L	M	I	s	R	T	P	E	V	•
		ACA	TGC	GTG	GTC	GTC	GA(CGTC	3AGC	CAC	GA/	AGAC	CCT	rgac	GTC	AAC	TTC	AAC	TGG	TAC		
	121	TGT	'AC	CAC	CAC	CAC	CTO	CAC	TC	GT	3CT	CTC	GG!	CTC	CAC	TTC	AAG	TTC	ACC	ATG		180
a		т	С	v	V	v	ם	v	s	н	E	D	P	E	v	ĸ	F	N	W	Y	V	-
			GGC	GTC	GAC	GT	GCA?	raan								GAG	CAG	TAC	AAC	AGC	ACG	242
	181		CCC	CAC	CTO	CAC	CGT	ATTA				•		CGCC	•	CTC	GTC	ATC	TTC	TCG	TGC	240
a		D	G	v	E	v	н	N	A	K	T	ĸ	P	R	E	E	Q	Y	N	s	T	•
	• • •	TAC	CG1	rgte	GT	CAGO	CGT	CTC	CAC	CGTY	CCT	GCA(CAC	GA(CTGC	CTC	TAA	'GGC	:AAC	GAG	TAC	
	241	ATC	GC I	ACAC	CAC	STC	GCA	GGA(GTG	GCA(GGA(CGT	GTY	CT	SAC	GAC	TTA	CCC	TTC	CTC	ATG	300
a		Y .	R	v	V	8	v	L	T	v	L	н	Q	D	W	L	N	G	K	E	Y	•
	204	AAC	TGC	CAAC	3GT(CTC	CAA	CAA	AGC	CCT	ccc	AGC	CCC	CATO	CGAC	SAA S	ACC	ATC	TCC	AAA:	recc	3.60
	301	TTC	ACC	GTTC	CA	GAG	GTT	GTT:	rcg	GGA	GGG'	rcg	GGG	GTA	CTO	TT	TGC	TAC	AGC	TTT	CGG	360
a		ĸ	C	ĸ	v	s	N	K	A	L	P	A	P	I	E	ĸ	T	I	S	ĸ	A	•
	261	AA	AGGG	GCA(3CC	CCG	AGA	ACC	ACA			CAC			CCC	ATC	CGG	GAT	GAC	CTC	ACC	420
	361	TT	rcc	CGT	CGG	GGC'	TCT'	TGG	rgt			•			GG'	rag	3GCC	CTA	CTC	GAC	TGG	420
a		ĸ	Ģ	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	T	-
	421	AAG	GAA(CA	GGT(CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA:	rcc	CAGO	GAC	TAC	GCC	GTG	480
		TTC	CTT	GT(CAC	GTC	GGA(CTG	GAC	GGA	CCA	GTT	rcc	GAA	GAT	NGG (STC(CTC	CTAC	SCG G	CAC	
a		K	N	Q	V	3	L	T	С	L	V	K	G	F	Y	P	S	D	I	A	V	•
	481	GAG	TG	GGA(GAG(CAA'	TGG	GCA(GCC	GGA	GAA	CAA(+	CTA	CAA	GAC	CAC	3CC1	rcc · · · ·	CGT	CTC	GAC	540
		CT	CAC	CCT	CTC	GTT.	ACC	CGT	CGG	CCT	CTT	GTT	GAT	GTT	CTG	GTG(CGG	AGG	3CA(CGAC	CTG	
a																					D	
	541		CGA	CGG	CTC	CTT	CTT	CCT	CTA	CAG	CAA	GCT	CAC	CGT	GGA	CAA	GAG	CAG	GTG(GCAC	GCAG	600
	342	AG				GAA	GAA	GGA	GAT	GTC	GTT	CGA	GTG	GCA	CCT	GTT	CTC	3TC(CAC	CGT	CGTC	
a																					Q	
	601				-+-			+				+			-+-			+			GAAG	660
		CC																			TTC	
a											H	E	A	L	H	N	H	Y	T	Q	K	•
	661	AG	CCT	CTC	CCT -+-	GTC	TCC	GGG +	TAA	-	684											
	- 			GAG							_											

FIG. 5 NH-Dde **Boc-IEGPTLRQWLA** ARA-GGG HN CO-GGGG-IEGPTLRQWLAARA tBu Pbf Boc tBu Pbf Boc Wang resin 2% H₂NNH₂/NMF `^{CO}-GGGG-IĘGPTLRQWLAARA .**AARA-**GGG-HN tBu ры Вос Pbf Boc (BrCH₂CO)₂O Wang resin țBu Țrt tBu Trt CO-GGGG-IEGPTLRQWL .**RA-**GGG-HN tBu Pbf Boc tBu Wang resin H-IEGPTLRQWLAARA-GGG-HN CO-GGGG-IEGPTLRQWLAARA-OH peptide 17b PEG 5000 H-IEGPTLROWLAARA -GGG-HN CO-GGGG-IEGPTLRQWLAARA-OH peptide 19

FIG. 6

FIG. 7

		XbaI								1	•	C		1							
	_	TCTA	GAT	TTG'	TTT	TAA	CTA	ATT	AAA	GA (GA	ATA	ACA	TAT	GGA	CA	AAC	TCA	CAC	ATGT	C
c	1	AGAT	CTA.	AAC.	AAA	ATT(GAT.	raa:	rtt	CTC	·+· CT	rat	TGT	ATA	CCT	'GTI	TTC	BAGI	CTG	TACA	G
	61	CACC	TTG'	TCC	AGC'	TCC	GA.	ACT	CCT	GGG	GG	ACC	GTC	AGT	CTI	CCI	CTI	icco	ccc	AAAA	: + 120
c	01	GTGG.	AAC.	AGG '	TCG	AGG (CCT	rga (GGA (ccc	CCC	rgg	CAG	TCA	GAA	GGA	GAA	\GGC	GGG	TTTT K	3
	121	CCAA	GGA	CAC	CCT	CAT	SAT	CTC	CCG	GAC	cc.	rga(ggt	CAC	ATG	CGI	GGT	rggi	'GGA	CGTG	Α
c	121	GGTT	CCT	GTG	GGA (GTA(CTAC	GAG	GCC	CTG	GG.	ACT	CCA	GTG	TAC	GCA	CCA	ACCA	CCT	GCAC'	
	101	GCCA	CGA	AGA	ccc	TGA	GT	CAAC	STT	CAAC	TG	GTA(CGT	GGA	CGG	CG1	`GGA	\GG1	rgca	TAAT	G
c	101	CGGT	GCT"	TCT(GGG/	ACT	CCAC	TT(CAAC	STTC	GAC	CAT	GCA	CCT	GCC	GCA	CCI	CCA	CGT	ATTA N	+ 240 C A -
	241			+			• • • •	 -	• • • •	• • •	+-			+				+			+ 300
c		GGTT																		GGAG L	
	301	CCGT		+				 -	· ·		+ •			+	• • •			+			+ 360
c																-	-			K	_
	361			+	• • •	• • •	4	 -	• • • •	• • • •	+-			+				+			+ 420
c		GGGA(TGGT(
	421		• • •	• • +	• • •	• • • •	4		• • • •		+-			+				+		• • • •	+ 480
c		TCCA(_																T (
	481			+ -			4	 -	· • • ·		+-			+				+			+ 540
c		CGGA0 L																		Q	
	541			+			+	 -	· • • ·		+-			+	• • •			+			+ 600
C		GCCI																		L L	
	601	ACAG																			G + 660
c		TGTC																		GAGG S	
	661			+			4	 -			+-			+				+	·		+ 720
c		ACTA(G	
	721			+	• • •			-			+-			+				+		• • • •	+ 780
С		TTCC																		ACGA A	
		1	Baml	HÍ 																	

 TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527H

FIG. 8

	~	l								•	•		•								
	1	TCTA	GAT	TTG	TTT	TAA	CTA	ATT	AAA	GGA	GGA	ATA	ACA	TAT	GGA	CAA	AAC	TCA	CAC	atgt	c
c	•	AGAT	CTA	AAC	AAA	ATT	GAT	TAA	TTT	CCT	CCT	TAT	TGT	ATA	CCT	GTI	TTG	AGT	GTG	TACA C	G
		CACC	TTG	TCC.	AGC'	TCC	GGA	ACT	CCT	GGG	GGG	ACC	GTC.	AGT	СТТ	CCT	'CTT	ccc	ccc		c
	61	GTGG	AAC	+ AGG	TCG.	AGG	CCT	+ TGA	GGA	CCC	· + ·	TGG	CAG	- · + TCA	GAA	GGA	GAA	+ · ·	GGG	 TTTT	+ 120 G
C			C																	K	
	121	CCAA		+				+			-+-			+				+			+ 180
C		K	D	T	L	M	I	S	R	T	P	E	V	T	C	V V	V	V	D	GCAC V	s ·
	181	GCCA	CGA	AGA	CCC'	TGA	GGT	CAA	GTT	CAA	CTG	GTA	CGT	GGA	CGG	CGI	'GGA	GGT +··	GCA	TAAT	G + 240
c		CGGT	CCT	TCT	GGG.	ACT	CCA	GTT(CAA	GTT	GAC	CAT	GCA	CCT	GCC	GCA	CCT	CCA	CGT		C
	241	CCAA	GAC.	AAA	GCC	GCG	GGA	GGA	GCA	GTA	CAA	CAG	CAC	GTA	CCG	TGI	GGT	CAG	CGT	CCTC	A
.c	241	GGTT	CTG'	rrr(CGG	CGC	CCT	CCT	CGT	CAT	GTT	GTC	CTG	CAT	GGC	ACA	CCA	GTC	GCA	GGAG	
		CCGT							-									_	-	L Cara	-
	301	GGCA	- 	+	• • •		• • • •	+			-+-			+				+			+ 360
С		٧	L	H	Q	D	W	L	N	G	K	E	Y	K	С	K	V	3	N	K	Ă·
	361	CCCT																			C + 420
c		GGGA L																		TGGT P	
	421	AGGT	GTA	CAC	CCT	GCC	CCC	ATC	CCG	GGA'	TGA	GCT	GAC	CAA	GAA	CCA	GGT	CAG	CCT	GACC	T + 480
c	721	TCCA	CAT	GTG	GGA	CGG/	GG'	TAG	GGC	CCT	ACT	CGA	CTG	GTT	CTT	GGT	CCA	GTC	GGA		A
		GCCT	GGT	CAA	AGG	CTT	CTA:	rcc	CAG	CGA	CAT	CGC	CGT	GGA	GTG	GGA	GAG	CAA	TGG	GCAG	c
_	481	CGGA	CCA	GTT.	TCC	GAA(GAT	AGG	GTC	GCT	GTA	GCG	GCA	CCT	CAC	CCT	CTC	GTT	ACC	CGTC	
С		CGGA	V GAA														-		_	•	P - ጥ
	541		• • •	+	• • -			+			-+-			+	• • •		• • •	+	· · ·		+ 600
C		E	N	N	Y	K	T	T	P	P	V	L .	D	3	D	G	S	P	F	L	Υ -
	601			+				+			.+.			+				+		• • • •	+ 660
c		TGTC																		GAGG S	
	661	TGAT																			A + 720
c		ACTA	CGT	ACT	CCG	AGA	CGT	GTT(GGT(GAT(GTG	CGT	CTT	CTC	GGA	GAG	GGA	CAG	AGG		T
		AAGG	TGG	AGG	TGG'	rggʻ	rat(CGA	AGG'	rcc(GAC'	TCT(GCG'	TCA	GTG	GCT	GGC	TGC	TCG	TGCT	G
	721	TTCC	ACC!	rcc.	ACC	ACC	ATA	GCT"	rcc	AGG	CTG.	AGA(CGC.	AGT	CAC	CGA	CCG	ACG	AGC	ACGA	
С														_						A	
	781	CACC		• • +				+			-+-			+				+			+ 840
c	•																			A	
					-	amH: 	_														
	841	GCGC							861												
		CGCG	TAT	rag.	AGC'	TCC	TAG	GC													

FIG. 9

		XbaI								•			•	J							
	1	TCTA		+	• • •	• • •		+			-+-			+				+		4	- 60
c		AGAT	CTA	AAC	AAA	ATT	GAT	TAA'	TTT	CCT	CCT	TATT	rgt.	ATA M	CTA	GCT'	TCC.	AGG	CTG/	AGACO	} } .
	61	GTCA	GTG(GCT	GGC	TGC'	TCG	TGC	rgg	CGG	rggʻ	TGGC	:GG	AGG	GGG'	rgg	CAT	rga(GGG	CCA	120
c	••	CAGT	CAC	CGA	CCG	ACG.	AGC.	ACG.	ACC(GCC/	ACC	ACCO	CC,	rcc	CCC	ACC	GTA	ACT	ccc	GGGT1	7
	121	CCCT	rcc	CCA	ATG	GCT	TGC.	AGC	ACG	CGC	AGG	GGG/	\GG	ceč,	rgg	GGA	CAA	AAC'	TCA	CACAT	r 100
c	+4+	GGGA	AGC(GGT	TAC	CGA	ACG'	TCG	rgc	GCG'	rcc	CCC1	CCC	GCC/	ACC	CCT	GTT	PTG.	AGT	GTGTA	١.
	101	GTCC																			_
c	191	CAGG'	rgg/	AAC	GGG	TCG	TGG.	ACT	rga(GGA	ccc	CCCI	rgg(CAG	rca.	AAA	GGA	GAA	GGG		נ
		AACC	CAAC	GGA	CAC	CCT	CAT	GAT	CTC	CCG	GAC	CCT	'GA	GT	CAC	ATG	CGT	GGT:	GGT(GAC	3
c	241	TTGG		CCT	GTG		GTA	CTA	GAG(GGC	CTG	GGG#	CT	CCA	3TG	rac(GCA	CCA	CCA		2
		TGAG																			
_	301	ACTC	GTY	CT	TCT	GGG	ACT	CCA	GTT(CAAC	3TTC	GACC	ATC	GCA(CCT	3CC	GCA	CT	CCA	CGTAT	r
C																			-	н 1	
	361	ATGC		+				+			-+-			+				+	• • •		420
c		TACG A																		V I	
	421	TCAC																			\ - 480
c	401	AGTG	GCAG	GGA	CGT		CCT	GAC	CGA	CTT	ACC	GTTC	CT	CAT	GTT	CAC	GTT	CCA	GAG		ľ
	481	AAGC																			
c	-	TTCG	GGA(GGG	TCG	GGG	GTA	GCT(CTT	TT G(GTA (GAGG	TT	rcg	GTT.	rcc	CGT	CGG	GGC'		}
	541	CACA	GGT									TGAC									4 ► 600
c	342	GTGT		CAT	GTG	GGA	CGG	GGG'	TAG	GGC	CCT	ACTO	GA	CTG	GTT	CTT	GGT	CCA	GTC		r
	601	CCTG	CCT	GGT	CAA	AGG	CTT	CTA'	rcc	CAG	CGA(CATO	GC	CGT	GGA	GTG	GGA	GAG	CAA'	rggg	: - 660
c	302	GGAC	GGA(CCA	GTT	TCC	GAA	GAT.	AGG	GTC	GCT(GTAC	3CG	GCA(CCT	CAC	CCT	CTC	GTT.		3
		AGCC																			
c	661	TCGG	CCT	CTT	GTT	GAT	GTT	CTG	GTG	CGG	AGG	GCAC	GA	CCT	GAG	CT	GCC	GAG	GAA		3
		TCTA	CAG	CAA	GCT	CAC	CGT	GGA	CAA	GAG	CAG	GTGC	CA	GCA	GGG	GAA	CGT	CTT	CTC.	ATGC?	r
	721	AGAT	GTC	GTT	CGA	GTG	GCA	CCT	GTT	CTC	GTC	CACC	CGT	CGT	CCC	CTT	GCA	GAA	GAG'	TACG	A.
C																				C	_
	781	CCGT		+				+			-+-			+				+			840
c		GGCA V	CTA(M	egt H	ACT E	CCG.	AGA L	CGT'(H	STT N	GGT(H	JAT(Y	T T	Q Q	K	S	L L	S S	L L	S	AGGCC	3 -
			Bar	nHI !																	
		GTAA	ATA	A TĠ	GAT	CC															

C

FIG. 10

	^	Dai																			
		TCTAG	ATT	TGI	TTT	'AAC	TAA	TTA	AAG	GAG	GAA	TAA	CAT	ATC	ATC	GA	AGG:	rcco	ACT	CTGC	
	1	AGATO		-+-		• • •	+				+			-+-				+		• • • +	60
C																				L R	•
	61	GTCAG																			120
c	-	CAGTO	ACC	GAC	CGA	CGA	GCA	CGA	CCA	CCI	CCC	CCA	CCC	CTC	TT	rtg.	AGT	GTG1	CACA		
-		CTTGC																			
	121			-+-			+				+			+ -				+		+	180
С																				5 K	•
	181	AGGAC																			240
c		TCCTC	TGG T	GAC L	STAC M	TAG	SAGO	GCC R	TGC T	GG/ P	ACT(E	CAC V	TG:	rac(C	CA(V	CCA V	CCA V	CCT	GCA(V	TCGG S H	•
		ACGAA	\GAC	CC1	rgac	GTC	AAC	TT	CAAC	CTG	GTA(CGT	GA	CGG	CGT	GGA	GGT	GCA'	raa?	rgcca	
	241	TGCTT	· · · ·	-+-	 _T(CAC	יייייני אוייוניני	·	יייי אוייריב	 22 <i>C</i> (• + • • ግልጥ(20 a (+	 2014	 CCT	···	+ • • CGT:	 ልጥጥ	···+ ACGGT	300
c		E	D	P	E	V	K	F	N	W	Y	V	D	G	V	E	V	Н	N	A K	-
	201	AGACA	AAC	CCC	CGC	GAC	GA	CA	GTA(CAA	CAG	CAC	GTA(CCG	rgt	GGT	CAG	CGT	CCT	CACCG	360
	301	TCTGT	TTC	CGG	CGCC	CTC	CTC	CGT	CAT	STT	GTC	GTG	CAT	GGC.	ACA	CCA	GTC	GCA	GGA	STGGC	
C								-												T V	
	361	TCCTC		+ .				-			-+-			+			• • •	+		+	420
c		AGGAC	GTC H	GT(CTC D	GAC(W	GA(CTT N	ACC(GTT(K	CCTY E	CATO Y	GTT K	CAC	GTT K	CCA V	GAG S	GTT N	GTT K	rcggg A L	; , -
		TCCC	AGC	ccc	CATO	CGA(GAA	AAC	CAT	CTC	CAA	AGC	CAA	AGG	GCA	GCC	CCG	AGA	ACC	ACAGG	
	421	AGGG1	rcgo	GG(GTA(GCT(TT	+ PTG(GTA	GAG	- + - GTT	rcge	 GTT	TCC	CGT	CGG	GGC	TCT	TGG'	rgtcc	480
C		P	A	P	I	E	K	T	I	3	K	A	K	G	Q	P	R	E	P	Q V	•
	481	TGTA		+				+			-+-			+				+		+	- 540
c		ACATO	etg(T	GA(L	CGG(P	GGG! P	PAG B	GGC R	CCT. D	ACT E	CGA L	CTG(T	GTT K	CTT N	ggt Q	CCA V	GTC S	:GGA L	CTG T	GACGG C I	; , .
																				GCCGG	;
	541	ACCA	GTT	rcc	GAA	GAT	AGG	GTC	GCT	GTA	GCG	GCA	CCT	CAC	CCT	CTC	GT1	PACC	CGT	CGGCC	600 :
C		V	K	G	F	Y	P	S	D	I	A	V	E	W	E	S	N	G	Q	PE	3 -
	601			+				+			-+-			+				+	• • •	CTACA	- 660
c		TCTT	GTT(N	GAT Y	GTT K	CTG(T	GTG T	CGG P	AGG P	GCA V	CGA L	CCT D	GAG S	GCT D	GCC G	GAC S	Ga/ F	IGAA F	.GGA L	GATGT Y S	[] -
		GCAA	GCTY	CAC	CGT	GGA	CAA	GAG	CAG	GTG	GCA	GCA	GGG	GAA	CGT	CTI	CTC	CATC	CTC	CGTG	
	661	CGTT	CGA	+ ርጥር	CCA	 ССТ	 GTT	+ CTC	GTC	CAC	CGT	CGT	CCC	CTI	GCA	GN	\GA(TAC	GAG	GCAC	F 720
С		K	L	T	V	D	K	S	R	W	Q	Q	G	N	V	P	3	С	3	V P	4 -
	721							+			. + -			4		• • •	• • • •	• + • •		TAAA	r /8U
c .	, 41	ACGT	ACT	CCG	AGA	CGT	GTT	GGT	GAT	GTG	CGT	CTT	CTC	:GGA	GAC	;GG/	ACA (GAGG	CCC	K	A
U ,		Bam		••			-•	- -	-	-	-										
		1		~~																	
	781	AATG																			
		TTAC	CTA	GG																	

FIG.11

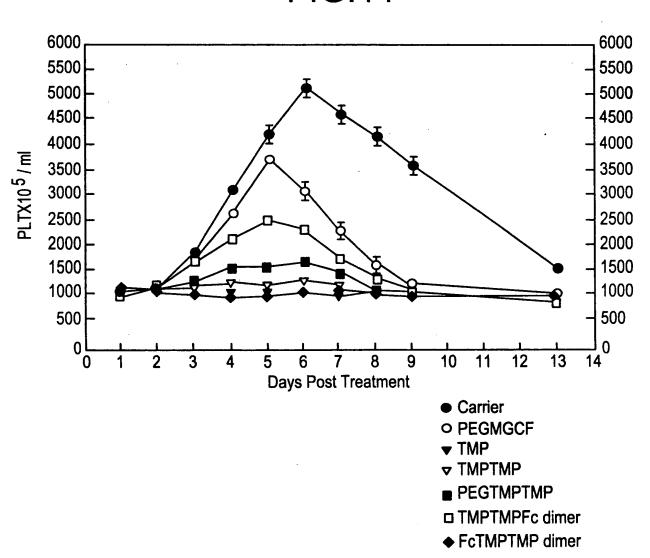
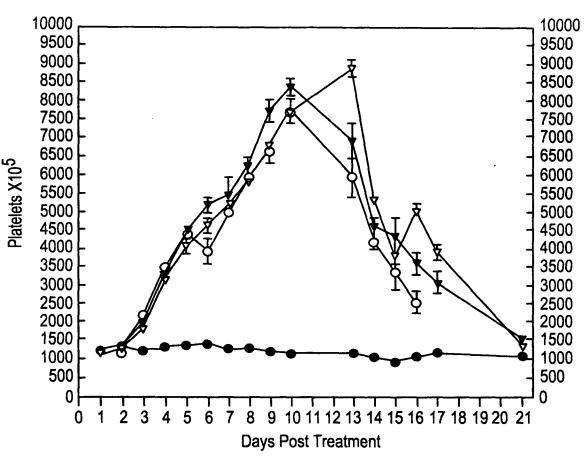


FIG.12



- Carrier
- o PEG MGDF
- ▼ TMPTMPFc dimer
- ▼ FcTMPTMP dimer

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527H

FIG. 13

	:	KbaI									ı		٠.	•	J	,						
	1	TCTA	GAT	TTG	TTT	TAA	CTA	ATT.	AAA	GGA	GGA	ATA	ACA	TAT	GGA	CAA	AAC	TCA	CAC	ATGI	rc .	
c	•	AGAT	CTA	AAC	AAA	ATT	GAT	TAA	TTT	CCT	CCT	TAT	rgt.	ATA	CCT	GTI	TTC	ag1	GTG	TACA	١G	
	61	CACC		+		• • •		+			-+-			AGT	CTT	CCI	CTI	rccc	ccc	AAA	۱Ċ	
c		GTGG.			TCG. A			TGA L	GGA L	CCC	G G	TGG(P	CAG S	TCA V	GAA F	GGA L	GAA F	AGGC P	GGG P	TTTT K	rG P	
	121	CCAA	GGA(CAC	CCT	CAT	GAT	CTC	CCG	GAC	CCC'	TGAC	GT.	CAC	ATG	CGI	GG1	GGT	GGA	CGT	SA.	100
c		GGTT	CCT(D	GTG	GGA	GTA	CTA	GAG	GGC	CTG	GGG.	ACTO	CA	GTG	TAC	GCA	CCA	ACCA	CCT	GCAC	T	
	101	GCCA	CGA	AGA	CCC'	TGA	GGT	CAA	GTT	CAA	CTG	GTA	CGT	GGA	CGG	CGI	'GG#	\GG1	rgca	TAAT	rG	
c	181	CGGT	GCT'	rc T	GGG.	ACT	CCA	GTT	CAA	GTT	GAC	CATO	CA.	CCT	GCC	GCA	CC1	CCA	CGT	ATT!	\C	
	241	CCAA	GAC	AAA	GCC	GCG	GGA	GGA	GCA	GTA	CAA	CAG	CAC	GTA	CCG	TGI	'GG1	CAC	CGT	CCTO	A	
c	241	GGTT	CTG	LTT	CGG	CGC	CCT	CCT	CGT	CAT	GTT	GTC	3TG	CAT	GGC	ACA	CC	IGT C	CGCA		T	
	301	CCGT	CCT	GCA(CCA	GGA	CTG	GCT	GAA'	TGG	CAA	GGA	STA.	CAA	GTG	CA	\GG1	CTC	CAA	CAA	AG	360
c		GGCA	GGA(CGT	CCT	CCT	GAC	CGA	CTT	ACC	CTT	CCT	TAS	GTT	CAC	GTI	CCI	\GA(GTT		C	
		СТССС																				420
c	301	GGGA	GGG'	rcg	GGG	GTA	GCT	CTT	TTG	GTA	GAG	GTT1	rcg	GTT	TCC	CGT	CGC	GGC	TCT		rg	
	421	AGGT																				400
c	421	TCCA		GTG	GGA	CGG	GGG'	TAG	GGC	CCT	ACT	CGAC	TG	GTT	CTT	GG1	CCA	\GTC	GGA		3A	
	481	GCCT																				540
c		CGGA	V	K	G	F	Y	P	S	D	I	A	V	E	W	E	3	N	G	Q	P	•
c	541		CTT	- · + GTT	GAT	GTT	CTG	+ · · CTG	cgg.	AGG	-+- GCA	CGAC	CT	+ GAG	GCT	GCC	GAC	GA/		• • • •	+ GA	
	601	ACAG		-								GCAG						CTC	ATG	CTC		660
C	601	TGTC	GTT	CGA	GTG	GCA	CCT	GTT	CTC	GTC	CAC	CGT	CT	ccc	CTT	GCA	\GAJ			GAG(3C	
		TGAT	GCA:	rga	GGC'	TCT	GCA	CAA	CCA	CTA	CAC	GCAG	SAA	GAG	CCT	CTC	CCI	rgto	CTCC	GGG1	A1	720
c	661	ACTA	CGT	ACT		AGA	CGT	GTT	GGT	GAT	GTG	CGT	CTT	CTC	GGA	GAG	:GGI	ACAC	SAGG		T	
	721	AAGG'		+				+		• • •	-+-			+		• • •	• • • •	+-•			+	780
c		TTCC.	ACC'	TCC. G	ACC. G	ACC. G	ACC' G	TCC. G	ATG. T	AAT(Y	GAG S	AAC(GT H	gaa P	GCC G	GGC P	CG/ L	ACT(SAAC W	V V	C	•
	•									Bami	HI											
		GCAA	ACC	GCA	GGG	TGG	TTA	ATC	TCG	TĠG.	ATC	C _										

GCAAACCGCAGGTGGTTAATCTCGTGGATCC
781
CGTTTGGCGTCCCACCAATTAGAGCACCTAGG
K P Q G G +

C

FIG. 14 XbaI C M G G T Y S C H -TGAAGCCGGGCGACTGAACCCATACATTCGGTGTTCCCCCACCCCCTCCGCCCCCCCTGT F G P L T W V C K P Q G G G G G G D K. C AAACTCACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCC 121 ------- 180 TTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGG C THTCPPCPAPELLGGPSVFL. TCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCG AGAAGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGC C FPPKPKDTLMISRTPEVTCV-TGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 241 -----+ 300 ACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGC V V D V S H E D P E V K F N W Y V D G V -C TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACACCACGTACCGTG ACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCAC EVHNAKTKPREEQYNSTYRV-C TGGTCAGCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA ACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGT c V S V L T V L H Q D W L N G K E Y K C K-AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGC 421 -----+ 480 TCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCG V S N K A L P A P I E K T I S K A K G Q c AGCCCCGAGAACCACAGGTGTACACCCTGCCCCATCCCGGGATGAGCTGACCAAGAACC TCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGG C PREPQVYTLPPSRDELTKNQ-AGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG TCCAGTCGGACTGGACGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCC C V S L T C L V K G F Y P S D I A V E W E -AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG TCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGC S N G Q P E N N Y K T T P P V L D S D G · c **GCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACG** CGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGC SFFLYSKLTVDKSRWQQGNV-C TCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT 721+ 780 AGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGA F S C S V M H E A L H N H Y T Q K S L S c

BamHI

CCCTGTCTCCGGGTAAATAATGGATCC 781 ----- 807 GGGACAGAGGCCCATTTATTACCTAGG LSPGK

c

FIG. 15 XbaI ь MGGTYSC CCACTTCGGCCCACTGACTTGGGTTTGCAAACCGCAGGGTGGCGGCGGCGGCGGCGGTGG GGTGAAGCCGGGTGACTGAACCCAAACGTTTGGCGTCCCACCGCCGCCGCCGCCGCCACC H F G P L T W V C K P Q G G G G G G b TACCTATTCCTGTCATTTTGGCCCGCTGACCTGGGTATGTAAGCCACAAGGGGGTGGGGG ATGGATAAGGACAGTAAAACCGGGCGACTGGACCCATACATTCGGTGTTCCCCCACCCC ь TYSCHFGPLTWVCKPQGGGG-AGGCGGGGGACAAAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGG TCCGCCCCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCC GGGDKTHTCPPCPAPELLGG ь ACCGTCAGTTTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGGCAGTCAAAAGGAGAAGGGGGTTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGG PSVFLFPPKPKDTLMISRTPb TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTG ACTCCAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGAC E V T C V V D V S H B D P E V K P N W ь GTACGTGGACGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA 361 -----+ 420 CATGCACCTGCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTT ь YVDGVEVHNAKTKPREEQYN CAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAA GTCGTGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTT ь STYRVVSVLTVLH.QDWLNGK GGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTC CCTCATGTTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAG ь YKCKVSNKALPAPIEKTIS CANAGCCANAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGA GTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACT KAKGQPREPQVYTLPPSRDE ь GCTGACCAAGAACCAGGTCAGCCTGACCTGCTGGTCAAAGGCTTCTATCCCAGCGACAT 601 -----+ 660 CGACTGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTA L T K N Q V S L T C L V K G F Y P S D · I b CGCCGTGGAGTGGGAGACAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGT 661 -----+----+- 720 GCGGCACCTCACCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCA A V E W E S N G Q P E N N Y K T T P P V ь GCTGGACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTG 721 -----+ 780 $\tt CGACCTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCAC$ LDSDGSFFLYSKLTVDKSRWь GCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC 781 -----+ 840 CGTCGTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTG Q Q G N V F S C S V M H E A L H N H Y T ь **RamHT**

Q K S L S L S P G K

b

FIG. 16 XbaI TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG C MDKTHTCP-CACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAAAAC 120 GTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAGGGGGGTTTTG P.C.PAPELLGGPSVFLPPPKP. c CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA 121 ------+ 180 GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGCACT K D T L M I S R T P E V T C V V V D V S. C GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATG 181 -----+ 240 CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC C HEDPEVKFNWYVDGVEVHNA. CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT c K T K P R E E Q Y N S T Y R V V S V L CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTC c V L H Q D W L N G K E Y K C K V S N K A -CCCTCCAGCCCCCATCGAGAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC 361 ------ 420 GGGAGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG c L P A P I E K T I S K A K G Q P R E P Q -AGGTGTACACCCTGCCTCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT 421 ------ +----- + 480 TCCACATGTGGGACGGAGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA Y T L P P S R D E L T K N Q V S L T C -C GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG C L V K G F Y P S D I A V E W E S N G Q P -CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT 541 -----+ 600 GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGA c BNNYKTTPPVLDSDGSFFL **ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGGGGGAACGTCTTCTCATGCTCCG** TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC C S K L T V D K S R W Q Q G N V F S C S V -TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGGACAGAGGCCCAT C MHEALHNHYTQKSLSPGK-AAGGTGGAGGTGGCGGAGGTACTTACTCTTGCCACTTCGGCCCACTGACTTGGGTTT 721 -----+ 780 TTCCACCTCCACCACCACCATGAATGAGAACGGTGAAGCCGGGTGACTGAACCCAAA C G G G G G G T Y S C H F G P L T W V C -GCAAACCGCAGGGTGGCGGCGGCGGCGGTGGTACCTATTCCTGTCATTTTGGCCCGC CGTTTGGCGTCCCACCGCCGCCGCCGCCACCATGGATAAGGACAGTAAAACCGGGCG c K P Q G G G G G G T Y S C H F G P L -TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC **ACTGGACCCATACATTCGGTGTTCCCCCAATTAGAGCTCCTAGG** C TWVCKPQGG

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527H

FIG. 17A

[<u>Aat</u>II sticky end] (position #4358 in pAMG21)

- GCGTAACGTATGCATGGTCTCC -
- 3' TGCACGCATTGCATACGTACCAGAGG-
- -CCATGCGAGAGTAGGGAACTGCCAGGCATCAAATAAAACGAAAGGCTCAGTCGAAAGACT --GGTACGCTCTCATCCCTTGACGGTCCGTAGTTTATTTTGCTTTCCGAGTCAGCTTTCTGA-
- -GGGCCTTTCGTTTATCTGTTGTTGTCGGTGAACGCTCTCCTGAGTAGGACAAATCCGC--CCCGGAAAGCAAAATAGACAACAAACAGCCACTTGCGAGAGGACTCATCCTGTTTAGGCG
- $\hbox{-} \hbox{CGGGAGCGGATTTGAACGTTGCGAAGCAACGGCCCGGAGGGTGGCGGGCAGGACGCCCGC}.$ -GCCCTCGCCTAAACTTGCAACGCTTCGTTGCCGGGCCTCCCACCGCCCGTCCTGCGGGCG-
- -CATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCTGACGGATGGCCTTTTTGCGT--GTATTTGACGGTCCGTAGTTTAATTCGTCTTCCGGTAGGACTGCCTACCGGAAAAACGCA -

<u>Aat</u>II - TTCTACAAACTCTTTTGTTTATTTTTCTAAATACATTCAAATATGGACGTCGTACTTAAC -- AAGATGTTTGAGAAAACAAATAAAAAGATTTATGTAAGTTTATACCTGCAGCATGAATTG -

- -TTTTAAAGTATGGGCAATCAATTGCTCCTGTTAAAATTGCTTTAGAAATACTTTGGCAGC -- AAAATTTCATACCCGTTAGTTAACGAGGACAATTTTAACGAAATCTTTATGAAACCGTCG-
- -GGTTTGTTGTATTGAGTTTCATTTGCGCATTGGTTAAATGGAAAGTGACCGTGEGCTTAC --CCAAACAACATAACTCAAAGTAAACGCGTAACCAATTTACCTTTCACTGGCACGCGAATG
- -TACAGCCTAATATTTTTGAAATATCCCAAGAGCTTTTTCCTTCGCATGCCCACGCTAAAC--ATGTCGGATTATAAAAACTTTATAGGGTTCTCGAAAAAGGAAGCGTACGGGTGCGATTTG-
- -GATAATTATCAACTAGAGAAGGAACAATTAATGGTATGTTCATACACGCATGTAAAAATA --CTATTAATAGTTGATCTCTTCCTTGTTAATTACCATACAAGTATGTGCGTACATTTTTAT -
- AACTATCTATATAGTTGTCTTTCTCTGAATGTGCAAAACTAAGCATTCCGAAGCCATTAT --TTGATAGATATATCAACAGAAAGAGACTTACACGTTTTGATTCGTAAGGCTTCGGTAATA-
- TAGCAGTATGAATAGGGAAACTAAACCCAGTGATAAGACCTGATGATTTCGCTTCTTTAA -- ATCGTCATACTTATCCCTTTGATTTGGGTCACTATTCTGGACTACTAAAGCGAAGAAATT -
- -TTACATTTGGAGATTTTTTATTTACAGCATTGTTTTCAAATATATTCCAATTAATCGGTG-- AATGTAAACCTCTAAAAAATAAATGTCGTAACAAAAGTTTATATAAGGTTAATTAGCCAC -
- -TTACTAACCTCAATCTTATTAGATGATATCCTAGTATAAAATAATTTAATCGCAGTAGTA-
- AATATTGCCTCCATTTTTTAGGGTAATTATCCAGAATTGAAATATCAGATTTAACCATAG -- TTATAACGGAGGTAAAAAATCCCATTAATAGGTCTTAACTTTATAGTCTAAATTGGTATC -
- AATGAGGATAAATGATCGCGAGTAAATAATATTCACAATGTACCATTTTAGTCATATCAG -- TTACTCCTATTTACTAGCGCTCATTTATTATAAGTGTTACATGGTAAAATCAGTATAGTC -
- ATAAGCATTGATTAATATCATTATTGCTTCTACAGGCTTTAATTTTTTTAATTATTCTGT -
- -GCAAGTTTTGCGTGTTATATATCATTAAAACGGTAATAGATTGACATTTGATTCTAATAA--CGTTCAAAACGCACAATATATAGTAATTTTGCCATTATCTAACTGTAAACTAAGATTATT-

FIG. 17B

- ATTGGATTTTTGTCACACTATTATATCGCTTGAAATACAATTGTTTAACATAAGTACCTG -
- TAACCTAAAAACAGTGTGATAATATAGCGAACTTTATGTTAACAAATTGTATTCATGGAC -
- -TAGGATCGTACAGGTTTACGCAAGAAAATGGTTTGTTATAGTCGATTAATCGATTTGATT-
- ATCCTAGCATGTCCAAATGCGTTCTTTTACCAAACAATATCAGCTAATTAGCTAAACTAA -
- CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGA
- -GATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCAATTGCGCAACCTTAAGCT -

SacII

- GCTCACTAGTGTCGACCTGCAGGGTACCATGGAAGCTTACTCGAGGATCCGCGGAAAGAA -
- CGAGTGATCACAGCTGGACGTCCCATGGTACCTTCGAATGAGCTCCTAGGCGCCTTTCTT -
- GAAGAAGAAGAAGCCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCAATA -
- CTTCTTCTTCTTCTTCGGGCTTTCCTTCGACTCAACCGACGACGGTGGCGACTCGTTAT -
- ACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGGTTTTTTGCTGAAAGGAGG
- -TGATCGTATTGGGGAACCCCGGAGATTTGCCCAGAACTCCCCAAAAAACGACTTTCCTCC-
- -AACCGCTCTTCACGCTCTTCACGC 3'

[SacII sticky end]

-TTGGCGAGAAGTGCGAGAAGTG 5'

(position #5904 in pAMG21)



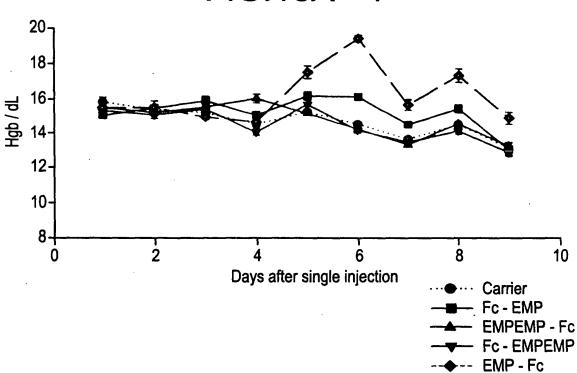


FIG.18A - 2

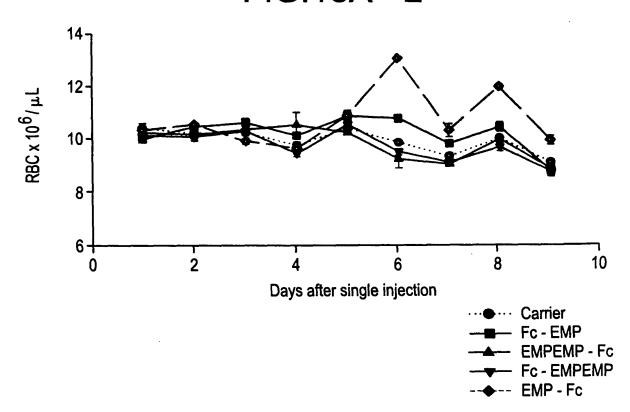


FIG.18A - 3

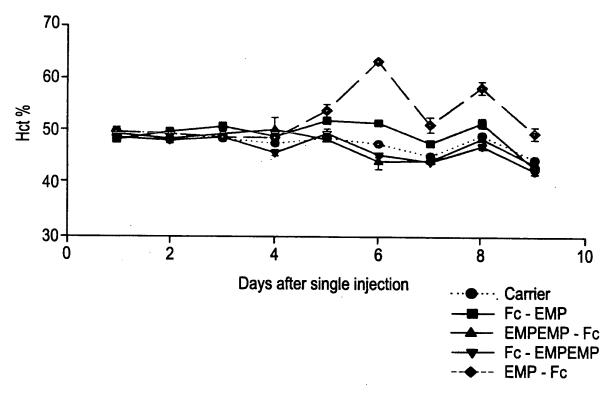


FIG.18B - 1

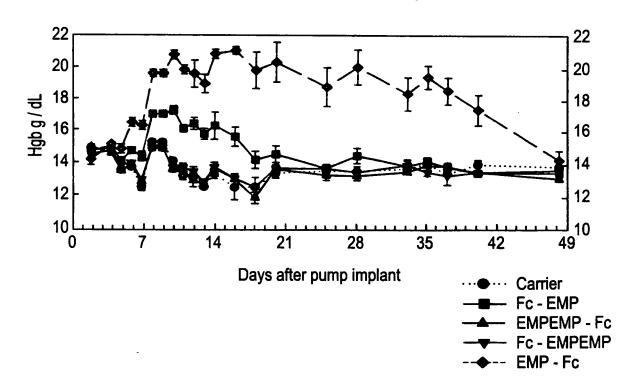


FIG.18B - 2

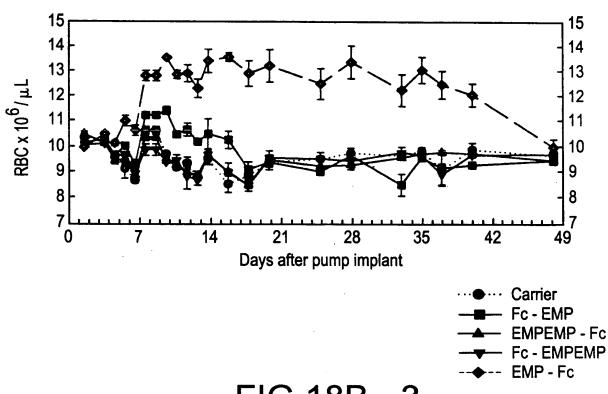


FIG.18B - 3

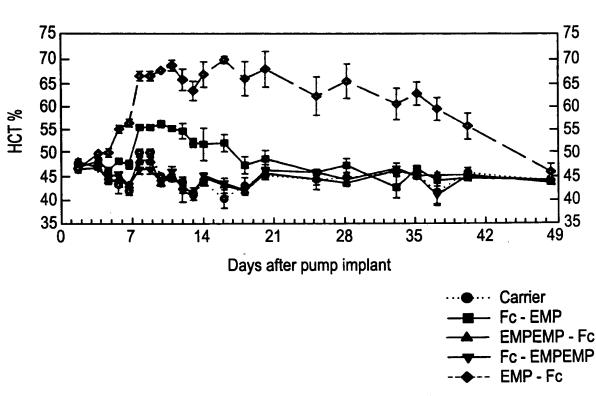


FIG. 19A NdeI CATATGGACAAAACTCACACATGTCCACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCG GTATACCTGTTTTGAGTGTACAGGTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGC M D K T H T C P P C P A P E L L G G P а TCAGTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 61 -----+ 120 AGTCAGAAGGAGAAGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTC SVFLFPPKPKDTLMISRTPE а GTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC 121 ------ 180 CAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG V T C V V V D V S H E D P E V K F N W Y а GTGGACGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCCTCCTCGTCATGTTGTCG V D G V E V H N A K T K P R E E Q Y N S a ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG 241 ------ 300 TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTC T Y R V V S V L T V L H Q D W L N G K E а TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAA 301 ------ 360 ATGTTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTT YKCKVSNKALPAPIEKTISK а GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG 361 -----+ 420 CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC A K G Q P R E P Q V Y T L P P S R D E L a ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC 421 ------ 480 TGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGG T K N Q V S L T C L V K G F Y P S D I A a GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG 481 -----+-----+ 540 CACCTCACCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGAC V E W E S N G Q P E N N Y K T T P P V L а GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG 541 -----+ 600 CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTC D S D G S F F L Y S K L T V D K S R W Q a

FIG. 19B

601				-+-			+				+			-+-			+			GCAG + CGTC	660
	Q	G	N	v	F	s	С	s	v	M	н	E	A	L	н	N	н	Y	T	Q	•
661				-+-			+				+			-+-	· · ·		+			CTAC + GATG	720
	K	S	L	S	L	s	P	G	K	G	G	G	G	G	מ	F	L	P	Н	Y	•
										Ва	ımH I										
721				CTC GAG			+				+		· • •	757	•						
	v	M	T	q	T.	G	н	R	P	*											

a

а

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527H

FIG. 20A

		Nd I	leI																			
	1	CAT	ATC	GAC	TTC	CTC	3CC	GCA(CTA	CAA	AAA	CAC	CTC	CT	GG1	CAC	CGT	'CCG	GGT	GGA	.GGC	60
	•	GTA	TAC	CTG	ÄAC	GAC	CGG	CGT	GAT	GTT	TTT	GTG	GAG	AGA	CCZ	AGTO	GCA	GGC	CCA	CCT	CCG	00
a			M	D	F	L	P	Н	Y	ĸ	N	T	s	L	G	Н	R	P	G	G	G	•
	<i>c</i> 1		GGG	GAC	:AA:	ACT	CA	CAC	A TGʻ	TCC	ACC'	TTG	CCC	AGC	ACCI	rga <i>i</i>	CTC	СТС	GGG	GGA	CCG	120
	61		CCC	CTC	TT	rtgi	AGT	GTG	TAC	AGG	TGG	AAC	GGG	rcg	rgg	ACTI	rgac	GAC	ccc	CCT	'GGC	120
a		G	G	D	ĸ	T	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	•
		TCA	GTI	rtt	CTC	CTTC	CCC	CCC							CAT	GAT	CTCC	cgc	ACC	CCI	GAG	100
	121	AGT	CA	AAA	GAG	SAA	GGG	GGG					GTG		GTA	CTA	GAG	GCC	TGC	GG?	CTC	180
a		s	v	F	L	F	P	P	K	P	K	D	T	L	M	ı	s	R	T	P	E	-
		GTC	CAC	ATG	CGT	GT(GGT	GGA	CGT	GAG	CCA	CGA	AGA	CCC	TGA	GGT	CAAC	3TTC	CAAC	CTGC	TAC	
	181	CAC	TG	rac	GCA(CA	CCA	+ CCT	GCA	CTC	GGT	+ GCT	TCT	GGG	· + · ACT	CCA	GTT(CAAC	STT	BAC	CATG	240
a		v	Т	С	v	v	v	D	v	s	н	E	D	P	E	v	K	F	N	W	Y	
		GTC	GAG	:GG(CGT	GGA(GGT	GCA	TAA	TGC	CAA	GAC	AAA	GCC	GCG	GGA	GGA(GCA(GTA(CAAC	CAGC	
	241				-+-			+				+			-+-			+			TCG	300
_		v	D	G	v	E	v	н	N		ĸ	т	ĸ	P	R	E	E	0	Y	N	s	
a		v 3.00	_	_	V	_	•					_		_		_	_	-	-	•	GGAG	
	301				-+-			+				+			-+-			+			CCTC	360
			JAT		ACA	- T	s	.GCA	.GGA	T	v	L	н	0	D	W	7.	N	G	ĸ	E	
a		т	¥	R	· ·	· ·	-	· ~ ·			•	_		-	_	•••	CAA		_		_	
	361				-+-			+				+			-+-			+			CAAA +	420
		AT	GTT(CAC	GTT	CCA				TC	:GGA	_	rrcg	_	_			_		GAG	GTTT	_
a		Y	K	С	K	V	S	N	K	A	L	P	A	P	I	E	K	T 	I 	3	K	•
	421				-+-			4				+			-+-			+			GCTG	480
																					CGAC	
a																					L	
	A Q 1				- 4 -							- +			+ -			+			CGCC	240
	401	ТG	GTT	CTT	GGT	CCA	GTC	:GG/	ACTO	GA(2GG <i>I</i>	ACCA	AGTI	TCC	GAA	GAT	AGG	GTC	GCT	GTA	.GCGG	+
a		T	ĸ	N	Q	v	3	L	T	C	L	V	K	G	F	Y	P	S	D	I	A	•
			GGA	GTG	GGA	GAG	CA	ATG	3GC <i>i</i>	AGC	CGG	AGA/	ACAZ	ACT!	ACA	\GAC	CAC	GCC	TCC	CGT	GCTG	600
	541	CA	CCT	CAC	CCI	CTC	GT:	rac	CCG	rcg	GCC	rct:	rgti	rga:	rgti	CTC	GTC	CGG	AGG	GCA	CGAC	:
a				W													T				L	•

FIG. 20B

601	• •			-+-			+				+			-+-			+			GCAG CGTC	660
	CT	GAG	GCT	GCC	GAG	GAA	-CAA	MOD	GAI	GIC	GII	CGA	GIG	GCA		GII	CIC	GIC	CAC		
	D	s	D	G	s	F	F	L	Y	S	K	L	T	V	D	K	3	R	W	Q	•
661		GGG	GAA	CGT	CTT				CGI											GCAG	72(
001		ccc	CTI	'GCA	GAA						CGT	ACT	CCG	AGA	CGI	'GTI	GGI	'GAT	GTG	CGTC	
	Q	G	N	V	F	s	С	s	V	M	Н	E	A	L	н	N	Н	Y	T	Q	-
										Ва	ımH I										
		GAG	CCI	CTC	CCI	GTC	TCC	:GGC	TA	AATA			rcc			:1					
721		CTC	GGA	GAC	GGA	CAC	AGC	CCC	CATT	rta?	•			•		, .					
		_		~			-	C	v												

FIG. 21A

	Nd	leI																				
	1	CAT	ATG	GAC	AA.	AAC	CA	CAC	ATGʻ	TCC	ACC'	TTG' +	rcc	AGC'	rcco	GA.	ACT	CTC	GGG	GG/	CCG	60
		GTA	TAC	CTC	TT	rtgi	AGT	GTG	TAC	AGG'	TGG.	AAC.	AGG'	TCG	AGG	CCT	rgac	GGA	CCC	CCI	GGC	
a			M	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	•
	61		GTC	TTC	CTC	CTT	CCC	CCC	AAA	ACC	CAA	GGA	CAC	CCT	CAT	GAT	CTC	CCG	GAC	CC1	GAG	120
	01		CAG	AAC	GAG	GAA(GGG	GGG	TTT'	TGG	GTT	CCT	GTG	GGA	GTA	CTA	GAG	GCC	CTG	3GG <i>I</i>	ACTC	120
a		s	v	F	L	F	P	P	K	P	K	D	T	L	M	I	s	R	T	P	E	•
	121			. .	+-			+				+			-+-			+			STAC	180
		CAG	TGI	'ACC	CAC	CCA	CCA	CCT	GCA	CTC	GGT	GCT	TCT	GGG.	ACT	CCA	GTT	CAA	GTT(GAC	CATG	
a		V	T	C	٧	v	V	D	V	s	Н	E	D	P	E	V	K	F	N	W	Y	-
	181				+ -			+				+			-+-			+			CAGC	240
		CAC	CTC	SCC	GCA	CCT	CCA	CGT	ATT	ACG	GTT	CTG	ттт	CGG	CGC	CCT	CCT	CGT	CAT	GTT(GTCG	
a		V	D	G	V	E	V	H	N	A	K	T	K	P	R	E	E	Q	Y	N	S	•
	241		. .		-+-			+				+			-+-		• • •	+			GGAG + CCTC	300
a		т	v	R	v	v	s	v	L	T	v	L	н	0	D	W	L	N	G	ĸ	Ē	-
a		_	*		" A A	con	-	CAA	_	_	•			-	САТ	CGA	GAA	AAC	САТ	CTC	CAAA	
	301				-+-			+				+		• • •	-+-			+			+ GTTT	360
a		Y	ĸ	С	ĸ	v	s	N	ĸ	A	L	P	A	P	I	E	K	T	I	s	K	•
	361				-+-			4			. .	. +			-+-			+			GCTG	420
		CG	GTT'	TCC	CGT	CGG	GGC	TCI	rtge	TGI	CCA	ACAI	GTG	iGG₽	CGG	GGG	TAG	GGC	CCT	ACT	CGAC	
a		A	K	G	Q	P	R	E	P	Q	V.	Y	T	L	P	P	S	R	D	E	L 	•
	421				-+-	·						- +			· - + -			+			CGCC + .GCGG	480
a																					A	
	481				-+-				+ •			• + • •			+ -							340
	401	CA	CCT	CAC	CCI	CTC	GTT	CAC	CCG	rcgo	GCC'	rct:	rgti	rg a ?	rgti	CTC	GTO	CGG	AGG	GCA	CGAC	
a		v	E	W	E	3	N	G	Q	P	E	N	N	Y	K	T	T	P	P	V	L	•
	541				- 4 -				+ ·			-+-			+ :						GCAG CGTC	300
a									L												Q	

a

FIG. 21B

	GT	CCC	CTT	GCA	GAA	GAG	TAC	GAG	GCA	CTA	CGT	ACT	CCG	AGA	CGT	GTT	GGT	GAT	GTG	CGTC	
	Q	G	N	V	F	s	С	s	V .	M	н	E	A	L	Н	N	Н	Y	T	Q	•
661				-+-			+				+			-+-			+			GGGT + CCCA	72
	K	S	L	s	L	s	P	G	K	G	G	G	G	G	F	E	W	T	P	G	-
										Ва	mHI 									•	
721				-+-			+	GCC CGG			+			-+-		763	,	•			

FIG. 22A

		1/4	aer	•																		
	1	CA	TAT	GTI	CGA	ATG	GA	CCC	CGGC	STT?	CTC	GGC1	AGC	GTA	CGC	TCI	'GCC	GCT	'GGG	TGG	AGGC	
	-	GT	ATA	CAA							GAC	CG	rcgo	CAI	GCC	AGA	CGG	CGA	ccc	ACC	TCCG	60
a			M	F	E	W	T	P	G	Y	W	Q	P	Y	A	L	P	L	G	G	G	-
	61	GG	TGG	GGA	CAA -+-	AAC	TC	ACAC	CATO	TCC	ACC	TTC	CCC	AGC	ACC	TGA	ACT	CCT	GGG	GGG	ACCG	120
		CC.	ACC	ССТ	GTI	TTG	AG	rgto	TAC	CAGO	TGC	AAC	GGG	TCC	TGG	ACT	TGA	GGA	CCC	CCC	TGGC	120
a		G	G	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	
	121	TC.	AGT	TTT	CCT	CTT	CCC	CCC	AAA	ACC	CAA	\GGA	CAC	CCT	CAT	GAT	CTC	CCG	GAC	CCC	TGAG	100
		AGʻ	TCA	AAA	GGA	GAA	.GGC	GGG	TTT	TGG	GTI	CCI	GTG	GGA	GTA	CTA	GAG	GGC	CTG	GGG.	ACTC	180
a		S	V	F	L	F	P	P	K	P	K	D	T	L	M	I	s	R	T	P	E	•
	181	GT	CAC	ATG	CGT	GGT	GGT	GGA	CGI	'GAG	CCA	CGA	AGA	CCC	TGA	GGT	CAA	GTT	CAA	CTG	GTAC	
															ACT	CCA	GTT	CAA	GTT	GAC	CATG	240
a		V	T	C	V	V	V	D	V	s	Н	E	D	P	E	v	ĸ	F	N	W	Y	-
	241					GGA		'GCA	TAA								GGA	GCA	GTA	CAA	CAGC	
	241							CGI	ATT						•	CCT	CCT	CGT	CAT	GTT	GTCG	300
a		v	D	G	V	E	V	Н	N	A	K	T	K	P	R	E	E	Q	Y	N	s	
	301	ACC				GGT										CTG	GCT	GAA'	TGG	CAA	GGAG	
	301	TG													•	GAC	CGA	CTT.	ACC	GTT	CCTC	360
a		T	Y	R	v	v	S	v	L	T	v	L	н	Q	D	W	L	N	G	ĸ	E	
	361	TAC	CAA	GTG	CAA	GGT	CTC	CAA		AGC					CAT	CGA	GAA.	AAC	CAT	CTC	CAAA	420
	301		3TT	CAC	GTT	CCA	GAG	GTT							GTA	GCT	CTT	TTG	GTA	GAG	GTTT	420
a		Y	K	С	K	V	S	N	K	A	L	P	A	P	I	E	K	T	I	s	K	•
	421															CCC.					GCTG	400
	701											-						•			CGAC	480
a		A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	-
	401																		CGA	CATO	CGCC	5.40
	481		•					-											GCT	GTA	CGG	540
a		T	ĸ	N	Q	v	s	L	T	С	L	v	K	G	F	Y	P	s	D	I	A	•
	C 4 1																				CTG	
	541																				CGAC	600
a	•	v	E	W	E	S	N	G	Q	P	E	N	N	Y	ĸ	T	T	P	P	v	L	•

FIG. 22B

	601	GA	CTC	CGA	CGG	CTC	CTI	CTI	'CCI	CTA	CAC	CAA	GCI	CAC	CGI	'GGA	CAA	GAG	CAG	GTG	GCAG	
	501	CT	GAG	GCT	'GCC	GAG	GAA	GAA	GGA	GAT	GTC	GTI	'CGA	GTG	GCA	CCI	GTT	CTC	GTC	CAC	CGTC	660
a		D	S	D	G	S	F	F	L	Y	S	K	L	T	V	D	K	s	R	W	Q	
	661	CA	GGG	GAA	CGT	CTI	CTC	ATC	CTC	CGT	'GA'I	GCA	TGA	GGC	TCI	GCA	CAA	CCA	CTA	CAC	GCAG	720
		GT	ccc	CTT	'GCA	GAA	GAG	TAC	GAG	GCA	CTA	CGT	ACI	CCC	AGA	CGI	'GTT	'GGT	'GAT	GTG	CGTC	, 20
a		Q	G	N	V	F	S	С	S	V	M	Н	E	A	L	н	N	Н	Y	T	Q	•
					•						Ва	ımHI I										
	721	• •			-+-			+				TAC			757	•			•			
											IMI	IAC	CIM	iGG								
a		ĸ	S	L	S	Ĺ	S	P	G	K	*											

FIG. 23A

	No	leI																				
	1				-+-		TCA	+			4		· ·	. .	+- •			-+-			+	60
		GTA	ATA(CCT	GTT'	rtg.	AGT	GTG:	rac;	AGG	rggc	CACC	GG7	rcg1	rgg <i>i</i>	CTI	GAG	GAC	CCC	CCT	GGC	
a			M	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	-
																			ACC	CCT	GAG	
	61						GGG											-	TGC	GGA	CTC	120
a		s	v	F	L	F	P	P	ĸ	P	ĸ	D	T	L	M	I	s	R	T	P	E,	-
		GTC	CAC	ATG	CGT	GGT	GGT	GGA	CGT	SAG	CAC	CGAZ	AGA	ccc:	rga(GT(CAAC	TTC	CAAC	TGG	TAC	
	121															CAC	TTC	CAAC	TTC	ACC	ATG	180
-		v	TP.	C.	v	v			v		н		D	P		v		F	N	W	Y	_
a		•			·	•	•	•													·	
	181		GA(CGG	CGT(GGA	GGT	GCA'				GACA +						CAC	TAC	CAAC	AGC	240
		CAC	CT	GCC	GCA	CCT	CCA	CGT	ATT	ACG	GTT(CTG	rtt(CGG	CGC	CCT	CTC	CGT	CATO	TTC	TCG	
a		V	D	G	V	E	V	H	N	A	K	T	K	P.	R	E	E	Q	Y	N	S	•
			STA	CCG																	GAG	200
	241		CAT	GGC																	CTC	300
a		т	Y	R	v	v	s	v	L	T	v	L	н	Q	D	W	L	N	G	к	E	-
		TAC	CAA	GTG	CAA	GGT	CTC	CAA	CAA	AGC	CCT	ccci	AGC	CCC	CAT	CGA	GAA	AAC	CATO	CTCC	CAAA	
	301				-+-			+				+			-+-			+ -		. .	+ 3TTT	360
_							s				L		•	P			ĸ	_	I	s	K	
a		Y		C		•	_				_	_		_	_	_		_	_	_	•	
	361				-+-	• • •		+				+		• • •	-+-			+				420
		CG	GTT	TCC	CGT	CGG	GGC	TCT	TGG	TGT	CCA	CAT	GTG	GGA(CGG	GGG'	TAG	GGC(CCT	ACTO	CGAC	
a		A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	-
	421						CAG		GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA	TCC	CAG	CGA	CAT	CGCC	480
	421																				GCGG	
a		T	ĸ	N	Q	v	s	L	т	С	L	v	ĸ	G	F	Y	P	s	D	I	A	-
		GТ	GGA	GTG	GGA	GAG	CAA	TGG	GCA	GCC	GGA	.GAA	CAA	CTA	CAA	GAC	CAC	GCC	TCC	CGT	GCTG	
	481				-+-			+				+			-+-			+			CGAC	540
																					L	
a																						
	541							+				+			-+-		-	+			GCAG	600
		CT	GAG	iGC 1	. GCC	GAC	JGA F	SCAP	(GGA	GAI	GIC	.GII	CGA	GIG	- C-		.			••••		
а		D	s	Q	G	S	F	F	L	Y	S	K	L	T	V	D	K	S	R	W	Q	•

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS INVENTORS: FEIGE et al.

INVENTORS: FEIGE, et al. APPLN. NO: A-527H

FIG. 23B

	601				· - + -	· -	· • • •	· +				+			-+-			+			GCAG + CGTC	660
3.		Q	G	N	V	F	S	С	s	V	M	Н	E	A	L	Н	N	Н	Y	Т	Q	•
	661				-+-			+	• • • •			+		• • •	-+-			+			TGAC + ACTG	720
à		K	S	L	S	L	S	P	G	K	G	G	G	G	G	v	E	P	N	c	D	-
																В	amH	I				
	721				-+-			+				TGA + ACT			-+-			+		77	3	
a		I	Н	v	M	W	E	W	E	C	F	E	R	L	*							

FIG. 24A

	N	deĮ																				
	CATATGGTTGAACCGAACTGTGACATCCATGTTATGTGGGAATGGGAATGTTTTGAACGT GTATACCAACTTGGCTTGACACTGTAGGTACAATACACCCTTACCCTTACAAAACTTGCA M V E P N C D I H V M W E W E C F E R CTGGGTGGTGGTGGTGACAAAACTCACACATGTCCACCGTGCCCAGCACCTGAACTC GACCCACCACCACCACCACCTGTTTTGAGTGTGTACAGGTGGCACGGGTCGTGGACTTGAG L G G G G D K T H T C P P C P A P E I																					
	•	GT.	ATA	CCA	ACT	TGG	стт	'GAC	ACT	'GTA	GGT	'ACA	ATA	CAC	CCT	TAC	CCT	TAC.	AAA	ACT'	TGCA	60
a			M	V	E	P	N	С	D	I	н	v	M	W	E	W	E	С	F	E	R	•
	61	CT	GGG	TGG	TGG	TGG	TGG	TGA	CAA	AAC	TCA	CAC	ATG	TCC	ACC	GTG	CCC.	AGC.	ACC'	TGA	ACTC	120
			CCC	ACC.	ACC	ACC	ACC	ACT	GTT	TTG	AGT	GTG	TAC	AGG	TGG	CAC	GGG'	TCG'	TGG.	ACT	TGAG	120
a		L	G	G	G	G	G	D	K	T	. Н	T	С	P	P	С	P	A	P	E	L	-
	121	CT	GGG	GGG.								CCC			CAA	GGA	CAC	CCT	CAT	GAT	CTCC	100
			CCC	CCC								•			GTT	CCT	GTG	GGA	GTA	CTA	GAGG	180
a		L	G	G	P	s	V	F	L	F	P	P	ĸ	P	K	D	T	L	M	ŗ	s	-
	181		GAC	CCC	TGA	GGT	CAC					GGA		GAG	CCA	CGA.	AGA	ccċ,	TGA	GGT	CAAG	240
	101		CTG	GGG.	ACT	CCA	GTG	•						CTC	GGT	GCT	TCT	GGĢ	ACT	CCA	GTTC	240
a		R	T	P	E	V	T	С	v	v	v	D	v	S	н	E	D	P	E	v	K	-
	241	TTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAG AAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCCTCCTC															200					
	241		GTT(GAC	CAT							•			•	CTG	TTT(CGG	CGC	ССТ	CCTC	300
3		F	N	W	Y	v	D	G	V	E	V	H	N	A	K	T	K	P	R	E	E	-
		CAC	ጌ ጥል(CAA	CAG	CAC	СТА	cce	ጥርጥ	<mark>ረረ</mark> ጥ	CAG	ረ ርጥ	ርርጥ	ሮልሮ	ርርጥ የ	ርርሞ(GC A	CCA	CCA	<u> የ</u> ጥርረ	GCTG	
	301				-+-			+				+			-+-			+			CGAC	360
a		0	Y	N	s	т	Y	R	v	v	s	v	L	т	v	L	н	0	D	w	t.	_
-		-	_		-	GTA	-		CAA	GGT	_	·	_	-	•	_		_	_	CGAC	GAAA	
	361	• •			-+-			+				+			-+-			+			TTT	420
a		N	G		E	Y		С		v					L	p	A	P	I	E	K	-
		AC	CAT	CTC	CAA.	AGC	CAA	AGG	GCA	.GCC	CCG	AGA	ACC.	ACA	GGT	GTA(CAC	CCT	GCC	CCC	ATCC	
	421				- + -	• • •		+		• • •		+			- + -			+	• • •		ragg	480
a																					s	-
		CG	3GA'	TGA	GCT	GAC	CAA	GAA	.CCA	.GGT	CAG	CCT	GAC	- CTG	CCT	GGT	CAA	AGG(CTT	CTA:	rccc	
	481				-+-			+				+			-+-			+	• • •		AGGG	540
3 .																					P	-
		AG	CGA(CAT	CGC	CGT	GGA	.GTG	GGA	GAG	CAA	TGG	GCA	GCC	GGA	GAA	CAA	CTA	CAA	GAC	CACG	
	541				-+-			+				+			-+-			+			GTGC	600
a																					T	-

FIG. 24B

	721	GT	GAT	GTG	CGT	CTT	CTC	GGA	GAG	GGA	CAG	AGG	ccc	ATI	TAT	• • •		+		77	3	
		C 3.	ama.	616		<i>~</i>	616				c.m.c	maa					Bami	Ī				
a		S	R	W	Q _.	Q	G	N	V	F	s	С	S	V	M	Н	E	A	L	Н	N	-
	661				-+-			+				+			-+-			+	·		GTTG	720
a		P AG	P						G												K CÁAC	•
	601			• • •	- + -			+		• • •		+			-+-			+	. 		CAAG + 'GTTC	660

FIG. 25A

	No	deI 																				
	1		• • •		-+-			+				+			-+-			+			ACCG + rggc	60
a			M	D	ĸ	T	н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
		TC	AGT	CTT	CCT	СТТ	ccc	ccc	AAA	ACC	CAA	.GGA	CAC	CCT	CAT	GAT	CTC	CCG	GAC	ccc	rgag	
	61				-+-			+				+			-+-			+			ACTC	120
a		s	v	F	L	F	P	P	K	P	ĸ	D	T	L	M	I	s	R	т	P	Ė	-
																					STAC	
	121																				CATG	180
a		v	T	С	v	v	v	D	v	s	Н	E	D	P	E	v	K	F	N	W	Y	
		GTO	GA(CGG	CGT	GGA	GGT	GCA	TAA	TGC	CAA	GAC	AAA	GCC	GCG	GGA	ĠGA	GCA(GTAG	CAAC	CAGC	
	181		 CCT(GCC	-+- GCA(CCT	CCA	+ CGT													TCG	240
a		v	D	G	v	E	v	н	N	A	K	T	ĸ	P	R	E	E	0	Y	N	S	-
		ACC	TAC	CCG:	rgto	GGT	CAG	CGT	CCT	CAC	CGT	CCT	GCA	CCA	GGA	CTG	GCT	- GAA'	rgge	CAA	GGAG	
	241				-+-			+				+			-+-			+			CTC	300
a		т	Y	R	v	v	s	v	L	т	v		н	0	ם		Ľ.	N	G	ĸ	E	-
		TAC	CAA	GTG	CAA	GGT	CTC	CAA	- Caa	AGC	CCT	ccc		-	_		- GAA				CAAA	
	301				-+-			+				+			-+-			+			TTT	360
a		Y	К	c	ĸ	v	s	N	ĸ	A	L	P	A	P	ī	Ė	ĸ	T	Ī	S	K	
		GCC	CAA	AGG	GCA	GCC	CCG	AGA	ACC	ACA	- GGT	GTA	CAC	CCT	GCC	CCC.	ATC	- CCG(- GGA:	rga(CTG	
	361			-,	- + -			+				+			-+-			+				420
a		A	ĸ	G	Q	P	R	E	P	Q	v	Y	T	L	P	P	S	R	D	E	L	-
		ACC	CAAC	GAAG	CCA	GGT	CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA	rcc	CAG	CGA	CATO	CGCC	
	421				-+-			+				+			-+-			+				480
a		т	K	N	0	v	s	L	т	С	L	v	ĸ	G	F	Y	P	s	D	I	A	
					_																CTG	
	481				-+-			+				+			-+-			+			CGAC	540
a																					L	•
•									-												GCAG	
	541				-+-			+				+			-+-			+			CGTC	600
a																					Q	

FIG. 25B

	601	CA	GGG	GAA	CGT	CTT	-														GCAG	
	001	GT	CCC	CTT	GCA	GAA															CGTC	
3.		Q	G	N	V	F	S	С	s	٧	M	Н	E	A	L	Н	N	Н	Y	T	Q	-
	661				-+-			+		·		+			-+-			+			GGGT	720
A.		ĸ			s	_						G							н		G	•
						Ва	IHm.	:														
	721				GTG -+- CAC			4		· ·	• • •	748	3						•			
a		F	T	L	c	*																

FIG. 26A

	No	ieI																				
	1	CAT	TATO	STG	CAC	CAC	CCA	CTG			CAC			CGGT	rgg <i>i</i>	AGGC	GG1	rggc	GAC	AAA	AGGT	60
	_	GT	ATAC	CAC	GTG	GTG	GGT	GAC	CCC	AAA	GTG	GGA(CAC	3CC!	ACC1	rcco	3CC#	ACCC	CTC	TT	CCA	
a			M	С	T	T	Н	W	G	F	T	L	С	G	G	G	G	G	D	K	G	-
	61			• • •	- + -			+				+			+	. .		- + -			GGGG + CCCC	120
a		G	G	G	G	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	• ,
	121				-+-			+				+			-+-		'-	+			GACC + CTGG	180
a		G	P	S	V	F	L	F	P	P	K	P	K	D	T	L	M	I	3	R	T	-
	181				-+-			+				+	• • •		-+-	• • •		+			CAAC + GTTG	240
a		P	E	v	T	С	V	V	V	D	V	S	Н	E	D	P	E	V	K	F	N	-
	241				-+-			+				+			-+-			+			GTAC + CATG	300
a		W	Y	v	D	G	V	E	V	н	N	A	K	T	K	P	R	E	E	Q	Y	•
	301				-+-			4				+			-+-			+	• • •		TGGC + ACCG	360
a		N	s	T	Y	R	v	V	S	V	L	T	V	L	H	Q	D	W	L	N	G	•
	361				-+-				 -			+			-+-			+			CATC GTAG	420
a		ĸ	E	Y	K	C	K	V	s	N	K	· A	L	P	A	P	I	E	K	T	I	•
	421								4 -			. +			-+-			+			GGAT + CCTA	480
a		3	ĸ	A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	•
	481				+ .				+			- +			+ -						GCTG	240
a		E.	L	T	K	N	Q	V	S	L	т	С	L	V	K	G	F	Y	P	S	D	•
	541								+			-+-			· - + ·						TCCC AGGG	000
а		r	A	v	E	W	E	S	N	G	Q	P	E	N	N	Y	K	T	T	P	P	-

FIG. 26B

	601	GT	GCT	'GGA	CTC -+-	CGA															CAGG	
		CA	CGA	CCT	GAG	GCT															GTCC	
a		V	L	D	s	D	G	s	F	F	L	Y	s	ĸ	L	T	v	D	ĸ	s	R	•
	661				-+-			+				+			-+-			+			CTAC	720
		AC	CGT	'CGT	CCC			GAA	GAG	TAC	GAG	GCA	CTA	CGT	'AC'I	'CCG	AGA	CGI	GTT	'GGT	'GATG	
a		W	Q	Q	G	N	V	F	S	С	S	V	M	Н	E	A	L	Н	N	Н	Y	•
													Ва	unHI 	•							
	721			GAA	-+-			+				+			-+-		763	3				
a		т	Q	K	s	L	s	L	s		G	K	*									